IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT: Herndon	§	**ART UNIT: 1614**
	§	
FILED: July 9, 2001	§	**EXAMINER: Kim, Vickie**
	§	
SERIAL NO.: 09/901,429	§	
	§	
FOR: β-Adrenergic Blockade Reversal Of Catabolism After Severe Burn	§	**DOCKET: D6414**
	§	

Assistant Commissioner of Patents
Washington DC 20231

TRANSMITTAL OF APPEAL BRIEF

Dear Sir:

Enclosed please find three originals of the Appeal Brief for the above-referenced patent application.

The Commissioner is hereby authorized to charge Deposit Account No. 07-1185 in the total amount of $160 for the appeal fee and any additional fee that may be required. Please credit any overpayment or debit any underpayment to Deposit Account 07-1185.

Respectfully submitted,

Date: Jan 15, 2003

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CERTIFICATE OF MAILING UNDER 37 CFR 1.8

Dear Sir:

I hereby certify under 37 CFR 1.8 that the following correspondence is being deposited with the United States Postal Service as first class mail with sufficient postage on the date indicated below and is addressed to Box AF, Assistant Commissioner of Patents, Washington DC 20231:

(1) Transmittal of Appeal Brief; and
(2) Three (3) copies of Appeal Brief.

Please return the enclosed postcard acknowledging receipt of this correspondence.

Respectfully submitted,

Date: Jan 15, 2003

Benjamin Aaron Adler, Ph. D., J.D.

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Assistant Commissioner of Patents
Washington, D.C. 20231

ATTENTION: Board of Patent Appeals and Interferences

APPELLANT'S BRIEF

This Brief is in furtherance of the Notice of Appeal filed in this case on December 11, 2002. In accordance with 37 C.F.R. §1.192(a), this Brief is submitted in triplicate. The fees required under 37 C.F.R. §1.17(c) and any other required fees are dealt with in the accompanying TRANSMITTAL OF APPEAL BRIEF.

INDEX OF SUBJECT MATTER

I. REAL PARTY IN INTEREST

The real party in interest is Research Development Foundation, the Assignee, as evidenced by an Assignment recorded in the Patent and Trademark Office at Reel 012938, Frame 0584 on May 28, 2002.

II. RELATED APPEALS AND INTERFERENCES

Appellant is aware of no other appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF THE CLAIMS

Originally claims 1-20 were filed with this Application. Claims 14-20 were withdrawn from further consideration by the Examiner as being drawn to non-elected inventions. Claims 8 and 13 were canceled. The pending claims 1-7 and 9-12 are being appealed of which claims 1 and 9 are independent claim.

IV. STATUS OF AMENDMENTS

Claims 1, 7 and 9 have been amended. No amendment was made in response to the Final Office Action mailed October 8, 2002. All pending claims are shown in Appendix A.

V. SUMMARY OF THE INVENTION

The present invention demonstrates that blockade of β-adrenergic stimulation with orally administered propranolol decreases resting energy expenditure and net muscle catabolism (page 3, line 12 to page 4, line 17; page 23, lines 10-14; Figure 2). Twenty-five acute, severely burned (>40% total body surface area) children were studied in a prospective, randomized trial. Thirteen of the subjects received oral propranolol for at least two weeks, and twelve served as non-treated controls. During beta blockade, heart rates and resting energy expenditures of the propranolol group were lower than baseline and lower than those of the control group ($p<0.05$). Corresponding to the significant differences in heart rate and resting energy expenditure, muscle protein net balance improved 82% relative to pre-treated baseline in the subjects treated with propranolol while it decreased

27% in the non-treated control subjects ($p<0.05$). These data indicate that propranolol attenuates hypermetabolism and reverses muscle protein catabolism in burn victims when administered for an extended period during acute hospitalization.

Thus, the present invention is drawn to a method of treating an individual having a severe burn by administering to the individual a pharmacologically effective dose of a beta-adrenergic antagonist, wherein treatment with the beta-adrenergic antagonist improves skeletal muscle protein kinetics in the individual as compared to individual without the treatment. In one embodiment, the beta-adrenergic antagonist is propranolol.

VI. ISSUES

35 U.S.C. §102(b)

Whether claims 1-7 and 9-12 are anticipated under 35 U.S.C. §102(b) by Herndon et al.

VII. GROUPING OF CLAIMS

The rejected claims stand or fall together.

VIII. ARGUMENTS

The Rejection Under 35 U.S.C. §102

In the Final Office Action mailed October 8, 2002, claims 1-7 and 9-12 were rejected under 35 U.S.C. §102(b) as being anticipated by Herndon et al. The rejection is respectfully traversed.

Claims 1 and 9 are drawn to methods of treating an individual having a severe burn, wherein said treatment with beta-adrenergic antagonist or propranolol improves skeletal muscle protein kinetics in said individual as compared to individual without the treatment (page 4, lines 8-12). In contrast, Herndon et al. taught that treatment with beta-adrenergic antagonist such as propranolol had no effect on protein metabolism in burn patients (see page 1301, Results section; page 1304, left column, second and third paragraphs). Herndon et al. did not teach or suggest treatment with beta-

adrenergic antagonist or propranolol would improve skeletal muscle protein kinetics in burn patients as claimed herein.

Applicant submits that the Examiner erred in asserting that "the cited reference meets all the critical elements required by the claims. Thus, all the claimed subject matter is anticipated by the cited reference" (Final Office Action, page 3). The methods claimed by the Applicant relate specifically to improved skeletal muscle protein kinetics in burn patients. In contrast, the cited Herndon et al. reference taught a method that had no effect on protein metabolism. Herndon et al. disclosed that "the rate of appearance of leucine, used as an index of total body protein catabolism, was not significantly altered by either β-blocker" (page 1301, last sentence of Results). Therefore, Herndon et al. taught a method that had no effect on protein metabolism. Herndon et al. clearly did not teach or suggest a method that would improve skeletal muscle protein kinetics as claimed herein.

The Examiner contended that "skeletal muscle kinetic improvement is naturally occuring when β adrenergic antagonists are administered to the patient with burns, and thus it is considered to be inherent feature" (Final Office Action, page 3, point 3). Applicant

submits that the Examiner's conclusion is without basis and directly contradicts with the teaching in Herndon et al. Herndon et al. concluded their study by stating that:

> In the present study, we failed to document an effect of propranolol and metoprolol on protein kinetics, although an earlier study indicted an increase in urea production with propranolol. That study used four patients who were aged 2 to 4 years, and the response in young children may differ from that in older children. It is also possible that the level of stress was higher. Finally, the short-term changes in urea production may not always correspond to changes in net protein breakdown. For this reason, in the present study, we used two independent approaches of assessing net protein breakdown. The fact that neither of these techniques revealed any significant effect of either agent on protein kinetics indicates that the effect is of minimal clinical concern.
>
> In summary, selective β1-adrenergic and nonselective adrenergic receptor blocking agents can significantly reduce heart rate and myocardial oxygen consumption in hypermetabolic burned patients without adversely affecting protein kinetics. (page 1304, left column, second and third paragraphs)

Hence, Herndon et al. clearly taught that treatment with β–adrenergic antagonists or propranolol had no effect on protein kinetics in the treated individuals. Herndon et al. did not teach or suggest treatment with β-adrenergic antagonists had an inherent feature of improving skeletal muscle protein kinetics. Furthermore, the Examiner's assertion that skeletal muscle protein kinetic improvement is an inherent feature of treatment with β adrenergic antagonists is not consistent with the teaching of Herndon et al.

The Examiner has not provided any scientific reference or experimental data that would allow one of ordinary skill in the art to conclude that skeletal muscle protein kinetic improvement is an inherent feature of treatment with β adrenergic antagonists. Applicant submits that in the absent of the data disclosed herein, one of ordinary skill in the art would have no basis to conclude that treatment with β adrenergic antagonists would improve skeletal muscle protein kinetic. Therefore, the Examiner has fallen victim to the insidious effect of hindsight syndrome wherein that which was taught in the invention by the Applicant is being used against its inventor.

In the Advisory Action mailed November 20, 2002, the Examiner contended that "improving muscle protein metabolism is inherently possessed feature whether the said pathway has been known (discovered) in the art or not." Applicant respectfully disagrees.

First of all, Herndon et al. clearly taught that treatment with β adrenergic antagonists or propranolol had no effect on protein kinetics. Herndon et al. did not teach or suggest treatment with β adrenergic antagonists would improve skeletal muscle protein kinetics as claimed herein. Therefore, in view of Herndon et al., one of ordinary skill in the art would have no reason to believe or suspect improving muscle protein metabolism is an inherent feature of treatment with β adrenergic antagonists. Neither did the Examiner provide any evidence that would support the inference that improving muscle protein metabolism is an inherent feature of treatment with β adrenergic antagonists.

Moreover, Applicant submits that instead of disclosing an inherent feature of treatment with β adrenergic antagonists, the present invention provides results that are unexpected in view of the

prior art. Herndon et al. taught that treatment with β adrenergic antagonists or propranolol had no effect on protein kinetics. In contrast, the claimed invention discloses that muscle protein net balance improved 82% relative to pre-treated baseline in subjects treated with propranolol while it decreased 27% in the non-treated control subjects ($p<0.05$). Consequently, in view of the prior art of Herndon et al., applicant submits that the claimed methods with the unexpected results are patentable.

The Examiner also contended in the Advisory Action that the feature of improving muscle protein metabolism is not considered in determining the patentability of claims 1-7 and 9-12 because a method of treating a burn patient and a method of improving muscle protein metabolism (catabolism) are two separate inventions in view of the restriction requirement imposed by the Examiner. Applicant respectfully disagrees.

Applicant further wants to point out that this rejection was not raised in the Office Action or Final Office Action. This rejection was raised for the first time in the Advisory Action. Hence, the Examiner was rejecting the claims based on a rejection against

which Applicant did not have any chance to respond to before the Final Office Action.

The non-elected claims are drawn to a method of using a beta-adrenergic antagonist to decrease protein catabolism and increase lean body mass in an individual. In contrast, claims 1-7 and 9-12 are drawn to methods of treating an individual having a severe burn with beta-adrenergic antagonist or propranolol because the treatment would improve skeletal muscle protein kinetics in the treated individual. Claims 1-7 and 9-12 are not drawn to nor recite limitation recited in the non-elected claims. Hence, Applicant submits that claims 1-7 and 9-12 do not fall in the realm of the subject matter of the non-elected claims.

In conclusion, a claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. The identical invention must be shown in as complete detail as is contained in the claim. In view of the fact that Herndon et al. clearly taught that treatment with β adrenergic antagonists or propranolol had no effect on protein kinetics in burn patients, whereas the present invention discloses treatment with beta-adrenergic antagonist or propranolol

would improve skeletal muscle protein kinetics in burn patients, the present invention is not anticipated by Herndon et al. Consequently, Applicant respectfully requests that the rejection of claims 1-7 and 9-12 under 35 U.S.C §102(b) be withdrawn.

Respectfully submitted,

Date: Jan 15, 2003

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CLAIMS ON APPEAL

1. (twice amended) A method of treating an individual having a severe burn, comprising the step of administering to said individual a pharmacologically effective dose of a beta-adrenergic antagonist, wherein treatment with said beta-adrenergic antagonist improves skeletal muscle protein kinetics in said individual as compared to individual without said treatment.

2. The method of claim 1, wherein said beta-adrenergic antagonist is administered intravenously.

3. The method of claim 2, wherein said beta-adrenergic antagonist is administered in a dose that decrease heart rate in said individual by about 25%.

4. The method of claim 2, wherein said beta-adrenergic antagonist is administered in a dose of from about 0.1 mg/kg of the body weight of the individual to about 10 mg/kg of the body weight of the individual.

5. The method of claim 1, wherein said beta-adrenergic antagonist is selected from the group consisting of propranolol, timolol, nadolol, atenolol, metoprolol, esmolol, nipradilol, carvedilol and acebutolol.

6. The method of claim 1, wherein said beta-adrenergic antagonist is propranolol.

7. (amended) The method of claim 6, wherein said propranolol is administered intraveneously in a dose of about 1 mg/kg of the body.

9. (twice amended) A method of treating an individual having a severe burn, comprising the step of administering to said individual a pharmacologically effective dose of propranolol, wherein treatment with said propranolol improves skeletal muscle protein kinetics in said individual as compared to individual without said treatment.

10. The method of claim 9, wherein said propranolol is administered intravenously.

11. The method of claim 9, wherein said propranolol is administered in a dose that decrease heart rate in said individual by about 25%.

12. The method of claim 9, wherein said propranolol is administered in a dose of from about 0.1 mg/kg of the body weight of the individual to about 10 mg/kg of the body weight of the individual.